

Sequence Listing

<110> Van Bruggen, Nicholas Ferrara, Napoleone

<120> Vascular Endothelial Cell Growth Factor Antagonists and Uses Thereof

<130> P1717

<140> US 09/218,481

<141> 1998-12-22

<160> 16

<210> 1

<211> 110

<212> PRT

<213> Homo sapiens

<400> 1

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val 1 5 10

Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser 20 25 30

Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
35 40 45

Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 80 85 90

Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 95 100 105

Ile Lys Arg Thr Val

<210> 2

<211> 110

<212> PRT

<213> Homo sapiens

<400> 2

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val

15 5 10 1 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser 20 Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser 55 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 105 Ile Lys Arg Thr Val 110 <210> 3 <211> 110 <212> PRT <213> Homo sapiens <400> 3 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val 15 10 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser 25 Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser 50 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile 75 65 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 85 80 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 100 Ile Lys Arg Thr Val

```
<210> 4
<211> 110
<212> PRT
<213> Homo sapiens
<400> 4
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
                    5
                                                            15
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser
                                       25
                  20
                                                            30
 Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                  35
 Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                  65
 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
                  80
                                                            90
 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu
                  95
                                      100
                                                           105
 Ile Lys Arg Thr Val
                 110
<210> 5
<211> 110
<212> PRT
<213> Homo sapiens
<400> 5
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
                                       10
Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser
Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                  35
                                                            45
Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser
                  50
                                                            60
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
```

70

75

65

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 80 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 95 100 Ile Lys Arg Thr Val <210> 6 <211> 110 <212> PRT <213> Homo sapiens <400> 6 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys 35 Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser 60 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile 70 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 85 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 100 Ile Lys Arg Thr Val 110 <210> 7 <211> 110 <212> PRT <213> Homo sapiens <400> 7 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val 10 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser

Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys

25

30

20

				35					40					45
Val	Leu	Ile	Tyr	Phe 50	Thr	Ser	Ser	Leu	His 55	Ser	Gly	Val	Pro	Ser 60
Arg	Phe	Ser	Gly	Ser 65	Gly	Ser	Gly	Thr	Asp 70	Phe	Thr	Leu	Thr	Ile 75
Ser	Ser	Leu	Gln	Pro 80	Glu	Asp	Phe	Ala	Thr 85	Tyr	Tyr	Cys	Gln	Gln 90
Tyr	Ser	Thr	Val	Pro 95	Trp	Thr	Phe	Gly	Gln 100	Gly	Thr	Lys	Val	Glu 105
Ile	Lys	Arg	Thr	Val 110										
<210> 8 <211> 110 <212> PRT <213> Homo sapiens														
<4003 Asp		Gln	Leu	Thr 5	Gln	Ser	Pro	Ser	Ser 10	Leu	Ser	Ala	Ser	Val 15

Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys 35 Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser 50 Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 100 105

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser

Ile Lys Arg Thr Val 110

<210> 9 <211> 118 <212> PRT <213> Homo sapiens <400> 9 Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 45 35 Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 55 Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser 105 95 100 Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 115 118 110

<210> 10 <211> 118 <212> PRT <213> Homo sapiens

His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 40 45

Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 50 55 60

Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser 65 70 75

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 80 85 90

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser 95 100 105

Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 115 <210> 11 <211> 118 <212> PRT <213> Homo sapiens <400> 11 Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr 20 25 Asn Tyr Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 40 Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 50 Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser 65 Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 80 85 Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr 95 100 Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 110 115 <210> 12 <211> 118 <212> PRT <213> Homo sapiens Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly 1 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 50 60

Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr 105 95 100 Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 115 110 <210> 13 <211> 118 <212> PRT <213> Homo sapiens <400> 13 Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly 5 1 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr 20 His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 50 Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser 75 65 Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 80 Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr 100 Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 115 110 <210> 14 <211> 118 <212> PRT <213> Homo sapiens <400> 14 Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr

20

Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 55 Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser 75 Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser 100 95 Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu 115 110 <210> 15 <211> 121 <212> PRT <213> Homo sapiens <400> 15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 45

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly

Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 55 60

35

Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 85

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn 105 95 100

Glu Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr 120 110 115

Leu 121

<210> 16 <211> 121 <212> PRT

<213> Homo sapiens

<400> 16

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly 1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr 20 25 30

His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 40 45

Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr 50 55 60

Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser 65 70 75

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 80 85 90

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn 95 100 105

Glu Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr 110 115 120

Leu 121